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EXAMINER

BAUSCH, SARA E L

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 04/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/078,278

Applicant(s)

WAGNER ET AL.

Examiner

Sarae Bausch

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 February 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 29-55 is/are pending in the application.
- 4a) Of the above claim(s) 52-55 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 29-51 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>02/05</u> | 6) <input checked="" type="checkbox"/> Other: <u>Detailed Action</u> |

DETAILED ACTION

1. Currently, claims 29-51 are pending in the instant application. Claim 52-55 have been withdrawn. All the amendments and arguments have been thoroughly reviewed but were found insufficient to place the instantly examined claims in condition for allowance. The following rejections are reiterated from the previous office action. Response to arguments follow. This action is **FINAL**.

2. Applicants comments set forth on pages 2-8 of the response mailed 2/25/2005 are noted and specific responses to applicant comments are addressed in section 6 below.

Maintained Rejections

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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5. Claims 29-44 and 46-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kigawa et al (US Patent 5965361 Oct 1999) in view of Nolan et al. (WO 99/22029 May 1999).

Kigawa et al. teach a method for detecting the presence of a double stranded target nucleic acid sequence using a probe/RecA complex (abstract). Kigawa et al. teach the use of a nucleic acid probe, typically a single stranded nucleic acid prepared by a virus, plasmid, or a cosmid, a probe DNA moiety excised from a vector, or probe from an oligonucleotide synthesizing method (instant claim 32) (see column 5, lines 64-67 and column 6, lines 1-10). Kigawa et al. teach probes with 90-95% homology to the target nucleic acid sequence and a length of 100 to 1500 bases but longer or short polynucleotide probe may be used (instant claim 33) (see column 6, lines 12-18). Further, Kigawa et al. teach nucleotide probes with a label, such as a fluorescent indicator, a radioactive label or a ligand that can be bound to a specific reporter molecule such as biotin and digoxigenin (instant claim 34) (see column 6, lines 23-28). Kigawa et al. teach the use of RecA protein with a detectable label or ligand, such as a fluorescent indicator, a chemiluminescent agent, an enzymatic label, a radioactive label, biotin or digoxigenin (instant claim 35-36, 39 and 41) (see column 6, lines 61-67). Kigawa et al. teach alternatively detecting the double-stranded target nucleic acid by allowing the probe/RecA complex to react with an anti-RecA antibody with or without a label or ligand (instant claim 40) (see column 10, lines 50-58). Kigawa et al. teach the hybridization reaction can be performed in the presence of another protein, such as a single-stranded binding protein, if necessary to accelerate the reaction (instant claim 44) (see column 9, lines 18-22). Kigawa et al. teach detecting the presence of the double stranded target sequence by detecting a fluorescent signal derived from the RecA protein having a fluorescent label included in the probe/RecA complex bound to the target sequence

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detected with a fluorescent microscope or flow cytometer (instant claim 42-43 and 46) (see column 10, lines 24-32). Kigawa et al. teach the use of the probe/RecA hybridization method to detect various types of chromosomal aberration such as deletion and insertion (see column 13, lines 18-21). Kigawa et al. does not teach the use of MutS protein with RecA for the detection of chromosomal aberrations.

Nolan et al. teach a method of detection of DNA polymorphisms including nucleotide polymorphisms, insertions, and deletions (page 1, line 6-7) that includes using an immobilized mismatch-binding protein-coated microspheres to bind fluorescently labeled, mismatch-containing DNA by flow cytometry (instant claims 42-43, 46 and 48) (page 4, lines 24-26). Nolan et al. teach genomic DNA amplified by PCR using fluorescently labeled nucleotide triphosphates (instant claim 31, 32 and 47) (page 4, lines 26-28). Nolan et al. teach microspheres bearing immobilized mismatch-binding protein and further teach mismatch binding proteins to include bacterial mismatch-binding protein, MutS, or any other protein that recognizes DNA base pair mismatches which can be immobilized on microspheres by physical absorption or by the use of an affinity tag which binds to an affinity partner immobilized on microspheres, such as biotin affinity tag and avidin/streptavidin binding partner (instant claim 34 and 36-38, 49-51) (page 5, lines 23-29 and page 6 Table).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the method of detecting the double stranded target nucleic acid using a probe/RecA complex by Kigawa et al. to include the MutS protein detection system as taught by Nolan et al. to improve the method of probe/RecA detection system by Kigawa et al. The ordinary artisan would have been motivated to improve the method of

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detecting the double stranded target nucleic acid sequence using the probe/RecA hybridization system by Kigawa et al. with the mismatch binding protein, MutS immobilized to microspheres taught by Nolan et al. because Nolan et al. teaches that the MutS immobilized detection system provides a high throughput, small volume, and washless method for detecting SNPs in DNA (page 4, lines 5-6). Further, the method of Nolan et al. allows for rapid scanning of mismatch DNA which would improve the detection of RecA/probe complex formation taught by Kigawa et al. The ordinary artisan would have had a reasonable expectation of success that the use of MutS could be used in the method by Kigawa et al. because Nolan et al. teach that the use of MutS immobilized onto microspheres for the detection of SNPs with flow cytometry provides multiparameter detection with excellent sensitivity in a homogenous assay format and multicolor fluorescent detection can be exploited for the simultaneous detection of dozens, or potentially hundred of analytes in a single sample (page 3, lines 9-14).

Response to Arguments

6. In response to applicants comments on page 3, section D, that the present invention would not be of any value in a setting where the test DNA and probe are perfectly matched because MutS binding cannot occur or where the two strands of ssDNA being allowed to anneal have homology of only 90 to 95% because either no binding of MutS will occur or if there is multiple, separate single base pair mismatches, too much binding will result, making the data uninterruptible. This response has been thoroughly reviewed by not found applicable to the instant pending claims because the method is not limited to identifying mutations using MutS only to detecting the presence of MutS bound to the DNA structure. If too much binding would

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occur with MutS, MutS would be bound the DNA structure and the binding of MutS to the DNA would be detected, as required by instant claim 1.

In response to applicant's argument, on page 5, 1st paragraph, that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Applicant's assert, on page 6, last three lines, that the types of deletions and insertions detectable by the Kigawa method are not the MutS-recognizable insertions or deletion of the present claims. Applicants further assert that it is highly improbable that the Kigawa method would permit one to distinguish such small deletions\insertions from the wild type sequence. Attorney's arguments have been thoroughly reviewed are not found persuasive absent evidence on the record, see MPEP 2145[R-2] which states: the arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). This should not be construed as an invitation for providing evidence. As further stated in the MPEP 716.01 regarding the timely submission of evidence:

A) Timeliness.

Evidence traversing rejections must be timely or seasonably filed to be entered and entitled to consideration. In re Rothermel, 276 F.2d 393, 125 USPQ 328 (CCPA 1960). Affidavits and declarations submitted under 37 CFR 1.132 and other evidence traversing rejections are considered timely if submitted:

(1) prior to a final rejection,

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- (2) before appeal in an application not having a final rejection, or
- (3) after final rejection and submitted
 - (i) with a first reply after final rejection for the purpose of overcoming a new ground of rejection or requirement made in the final rejection, or
 - (ii) with a satisfactory showing under 37 CFR 1.116(b) or 37 CFR 1.195, or
 - (iii) under 37 CFR 1.129(a).

The claims are broadly drawn to mutations or SNPs and are not limited to the detection of only one single nucleotide polymorphism. Further, applicants assert on page 7, that Kigawa says nothing about using RecA for distinguishing SNP-containing sequences from “wild-type” sequences, however the claims are not limited to distinguishing only one SNP-containing sequences, the claims are broadly drawn to a method of detecting a mutation and/or a SNP in a double-stranded test DNA molecule, which encompasses the method of using RecA hybridization to detect chromosomal aberrations as taught by Kigawa.

Applicants assert on page 8 of the response mailed on 02/25/2005 that the method of Kigawa teaches away from the present invention because a person of ordinary skill in the art would appreciate that a homology of at least 90% to 95% with the target nucleic acid sequence would make impossible SNP/mutation detection using MutS or would generate false positives. Applicants further assert that the probe of the present invention is designed to avoid successful homology searching unless there is nearly perfect homology. This response has been thoroughly reviewed but was not found persuasive because Kigawa does teach identification of mutations with homology of at least 90% to 95% with the target nucleic acid sequence (see column 6, lines 12-13) and one of ordinary skill in the art would recognize that the method of Kigawa could be used to determine more than 90% homology to the target sequence, which would include single point mutations, since Kigawa teaches a probe with homology of at least 90% to 95% of target

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sequence. Furthermore, coupled with teachings by Kigawa of detecting specific genes and determining chromosomal ploidy and detecting chromosomal aberrations, such as deletions, insertions (see col. 13, lines 17-20), a person of ordinary skill in the art would understand that deletions, insertions encompass mutations or mispairing that MutS would identify. The claims are drawn to a method of detecting a mutation and/or SNP in a target sequence and “a mutation” broadly encompass several differences in a sequence, including deletions and insertions as recited in claim 2 wherein the mutation being detected is the addition or deletion of 1-4 nucleotides. Four mutations within the target sequence would entail 90% or 95% homology to the target sequence depending on the size of the target sequence and therefore Kigawa teaches a method of detecting a mutation using RecA and does not teach away from the present invention.

Applicants assert, on page 8, section 2, that Kigawa fails the “suggesting” test because Kigawa never suggests using oligonucleotides of different sequences than the target DNA to create an intentional mismatch. This argument has been thoroughly reviewed but was not found persuasive since the claims are not drawn to using oligonucleotides of different sequence than the target DNA to create an intentional mismatch nor are the claims limited to a probe that contains a single mismatch. The instant claims are drawn only to a method of detecting a mutation and or SNP wherein the probe has a known nucleotide sequence or a sequence complementary to the sequence of at least a part of the test DNA but the claims do not recite that the probe must contain an intentional mismatch of the test DNA. Furthermore applicants assert in section 1 on page 8 of the response that “Kigawa prefers probes with sequence identity and will accept probes with homology of at least 90% to 95% with the target nucleic acid sequence” and therefore the response acknowledges that Kigawa’s inventors aren’t striving to use probes

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that are identical to the target sequence and further the response acknowledges in this section that Kigawa uses oligonucleotides of different sequences from the target DNA.

Applicants assert, on page 8, section 2, that Kigawa inventors strive to use probes that are identical to the target sequence that they are attempting to detect and it is only logical that this reference does not suggest or motivate one to look to the MutS literature for any reason. This argument has been thoroughly reviewed but was not found persuasive because Kigawa teaches using probes that are at least 90% - 95% homologous to the target sequence (column 6, lines 12-13), which indicates mutations between the target sequence and the probe. Nolan et al. teach using MutS to detect mismatch-containing heteroduplex DNA (see page 2, lines 18-20) and therefore one would be motivated to look to the MutS literature as MutS recognizes mutations and Kigawa et al. teach mismatches between the probe and target sequence.

On page 9, section 3, Applicants assert that the method of Kigawa requires removal of the unreacted probes and the present method generates only positive signal when two or more components are co-localized and the positive signal depends upon target DNA, MutS and RecA and/or oligonucleotide. This argument has been thoroughly reviewed but not found persuasive as the claims recite a method "comprising" steps; additional step are encompassed by the claims. The claims are drawn to a method comprising a probe, MutS, and/or RecA that are labeled and the association is indicative of the presence of a mutation but the claims do not require that the method does not remove unreacted probes prior to detection. Further, in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re*

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Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

On page 9, section 4, applicants assert that the secondary reference of Nolan does not fill any gaps left by Kigawa and there is no suggestion in Nolan that the three-stranded structure formed by RecA homology could be a substrate for MutS binding or to combine the MutS method with any RecA based method. This response has been thoroughly reviewed but not found persuasive since the claims are not drawn to MutS recognizing the three stranded structure formed by RecA, the claims only require that the MutS binds to one or more base pair mismatches present in the duplex portion of D-loop structure or in the four stranded DNA structure, which only requires a duplex structure which is taught by Nolan. Furthermore, the ordinary artisan would have been motivated to improve the method of detecting the double stranded target nucleic acid sequence using the probe/RecA hybridization system by Kigawa et al. with the mismatch binding protein, MutS immobilized to microspheres taught by Nolan et al. because Nolan et al. teaches that the MutS immobilized detection system provides a high throughput, small volume, and washless method for detecting SNPs in DNA (page 4, lines 5-6) and Kigawa et al. teach a method of detecting target nucleic acid with mutations using RecA. Further, the method of Nolan et al. allows for rapid scanning of mismatch DNA that would improve the detection of RecA/probe complex formation taught by Kigawa et al.

On page 9, section 4, Applicants assert that Nolan focused on fluorescently labeled target DNA and never suggested detecting or labeling MutS. Applicants further argue that the Office is using hindsight reasoning in crafting the rejection as it relies on the present inventors teachings to pick and choose unrelated pieces of prior art to reconstruct the unobvious invention that

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Applicants have made. This argument has been thoroughly reviewed but is not found persuasive. First, Nolan does teach a method wherein MutS is labeled with a biotin affinity tag (see page 5, lines 27-28). Claim 29 is broadly drawn to method wherein MutS is optionally detectably labeled and optionally immobilized, which does not require that either occur. Furthermore, claim 34, 36-38, 49-51 are broadly drawn to method wherein MutS is labeled, but are not limited as to how MutS is detected. Nolan et al. teach a method wherein the immobilized MutS bound to DNA is detected by being labeled with a biotin affinity tag and immobilized on to microspheres. Second, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Lastly, applicants argue that the Office chose unrelated pieces of prior art to reconstruct the unobvious invention. This argument has been thoroughly reviewed but not found persuasive as it would have been obvious to one of skill in the art to use MutS to detect a mutation because Kigawa teaches using probes that are at least 90% - 95% homologous to the target sequence (column 6, lines 12-13), which indicates mutations between the target sequence and the probe. Nolan et al. teach using MutS to detect mismatch-containing heteroduplex DNA (see page 2, lines 18-20) and therefore one would be motivated to look to the MutS literature as MutS recognizes mutations and Kigawa et al. teach mismatches between the probe and target sequence. As stated in the MPEP 2145, section IX, a prior art reference is analogous if the reference is in the field of applicant's endeavor or, if not, the reference is reasonably pertinent to

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the particular problem with which the inventor was concerned. In re Oetiker, 977 F.2d 1443, 1446, 24 USPQ2d 1443, 1445(Fed. Cir. 1992). Both MutS and RecA are DNA repair enzymes. References directed to such are not unrelated pieces of art.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

7. Claim 45 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kigawa et al (US Patent 5965361 Oct 1999) in view of Nolan et al. (WO 99/22029 May 1999) as applied to claims 29-44 and 46-51 above in section 4, and further in view of Olson et al. (US Patent 5888728 March 1999).

The method of Kigawa et al. in view of Nolan et al. is set forth in section 4 above. Kigawa et al. in view of Nolan et al. does not teach the use of SSB protein labeled with a detectable label.

Olson et al. teach streptavidin bound to biotinylated SSB in order for the complex (SSB-oligonucleotide) to bind to a capture membrane (see column 5, lines 39-50 and 55-60).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the method of Kigawa et al. in view of Nolan et al. of detecting a mutation in a double stranded test DNA molecule with a probe/RecA complex bound to the test DNA and contacting the DNA with MutS protein to detect the presence of MutS bound to the DNA structure with SSB to include a labeled SSB protein as taught by Olson et al. to improve the detection of the mutation in the target DNA. The ordinary artisan would have been motivated to improve the method of Kigawa et al. in view of Nolan et al. to include a labeled SSB protein because Olson et al. teach that the assay can be performed

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with many combinations of sequential assays(see column 4, lines 36-39). Furthermore, Olson further teaches that many complexes may be formed and these complexes may have one or more components and the assay can be designed to avoid interference from specific substances (see column 4, lines 59-65), therefore the ordinary artisan would have had a reasonable expectation of success to include a labeled SSB, in the method of Kigawa et al. in view of Nolan et al.

Response to Arguments

8. Applicants asserts, on page 10, 2nd paragraph, that because the combination of Kigawa with Nolan does not give rise to a legally sufficient basis for prima facie obviousness rejection the addition of yet another disconnected reference to that mix and its application against claim 45 does not cure the inadequacy of the primary or secondary references or their combination with respect to claim 45. Applicants assert that neither Kigawa, Nolan nor their combination can be said to suggest the use of SSB or a need for anything like SSB and Olson does not suggest using SSB with D loop structures formed by RecA alone or with D-loops and mismatches recognized by MutS to help detect SNPs or mutations. These arguments have been thoroughly reviewed but not found persuasive because the method of detecting target nucleic acid sequence by Kigawa does teach the use of SSB to accelerate the reaction of the probe with RecA (see column 8, lines 35-39). The method of Kigawa in view of Nolan does not teach the use of labeled SSB and one would be motivated to use the method of a labeled SSB protein as taught by Olson because Olson et al. teach that the assay can be performed with many combinations of sequential assays (see column 4, lines 36-39) and that many complexes may be formed and these complexes may have one or more components and the assay can be designed to avoid interference from specific

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substances. For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

9. On page 10, last paragraph, Applicants argue that the primary reference cannot be considered an adequate legal basis for a prima facie obviousness rejection because it teaches away from the present invention and does not suggest looking to the secondary reference. This response has been thoroughly reviewed and not found persuasive for the reasons set forth above in section 6 of this action. The response argues that the primary reference does not suggest looking to the secondary reference and further states that Nolan does not suggest that the three-stranded structure formed by RecA and dsDNA could be a substrate for MutS, this argument has been thoroughly reviewed but was not found persuasive. As noted in the MPEP 2143.01, in *Ruiz v. A.B. Chance Co.*, 357 F.3d 1270, 69 USPQ2d 1686 (Fed. Cir. 2004), the court rejected the notion that “an express written motivation to combine must appear in the prior art references...”. With regard to applicants argument that there is no suggestion in either of Kigawa or Nolan to consider using the SSB protein, see section 8 of this action. As stated previously, the method of detecting target nucleic acid sequence by Kigawa does teach the use of SSB to accelerate the reaction of the probe with RecA (see column 8, lines 35-39). For these reasons, and the reasons made of record in the previous office actions, the rejections are maintained.

Conclusion

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sarae Bausch whose telephone number is (571) 272-2912. The examiner can normally be reached on M-F 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

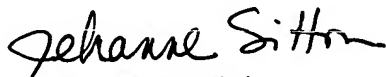
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Any inquiry of a general nature or relating to the status of this application
or proceeding should be directed to (571) 272-0547.

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JEHANNE SIFTON
PRIMARY EXAMINER
4/4/05


Sarah Bausch
Examiner
Art Unit 1634